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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/961,376	09/25/2001	Steven M. Ruben	PF524P1	6600

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EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 05/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/961,376	RUBEN ET AL.	
	Examiner	Art Unit	
	Prema M Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,22,23,25-28,31,33,34,36 and 38-75* is/are pending in the application.

4a) Of the above claim(s) *1, 22, 23, 25-28, 33, 34, 39-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31,36 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 11/5/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group VIII (claims 31, 36 and 38, species of Sjogren's Syndrome) on 3/8/2004 is acknowledged. The traversal is on the ground(s) that the search and examination of Groups V, VIII and IX would not entail a serious burden. This is not found persuasive because Group V is drawn to a method for treating an immunodeficiency condition (lack of a proper immune response) comprising administering a TR17 antibody, Group VIII is drawn to a method of treating an autoimmune condition (an immune response against the patient's self antigens) comprising administering a TR17 antibody and Group IX is drawn to a method of killing cells comprising administering a TR17 antibody. Each Group represents an independent and distinct invention because a search for a method of administering TR17 antibody for treating an autoimmune condition would not necessarily reveal art for a method of treating an immunodeficiency condition. Therefore, Applicants argument that a single search may be sufficient to permit examination for all three groups, is non-persuasive. If the elected species of the Markush group (Sjogren's Syndrome) is found allowable, the examination will be extended until at least one member of the Markush group is found not to be allowable.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1, 22-23, 25-28, 33-34, 39-75 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. It is suggested that the title be changed to reflect the recited method.

Claim Rejections - 35 USC § 101/112, first paragraph

3. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31, 36-37 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The disclosed utilities for the asserted TR17 polypeptide as a novel member of the tumor necrosis factor family of receptors include TR17 inhibition of B cell proliferation in an in vitro co-stimulatory assay (see Example 14, page 296-297), enhancement of T cell proliferation (see Example 15, page 297-298), effect of TR17 on the expression of MHC Class II costimulatory and adhesion molecules and cell differentiation of monocytes and monocyte-derived human dendritic cells (see Example 16, pages 298-300), the effect of TR17 on the growth of vascular endothelial cells (see Example 17, page 300-301), and the stimulatory effect of TR17 on the

proliferation of vascular endothelial cells (see Example 18, page 301). However, neither the specification nor any art of record teaches specifically how an antibody to TR17 could be so used. The specification merely discloses that because TR17 may be a member of the TNF family of receptors and because the extracellular cysteine rich motifs of TR17 disclosed in Figure 1 are important for interactions between TR17 and its ligands (see page 13, [0046]), an antibody to TR17 may be useful.

Furthermore, the instant claims are drawn to a method of using an antibody to a polypeptide, which has an as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as having homology to the TNF family of receptors (page 1, [0002]), the instant invention is incomplete. The instant specification does not disclose any information regarding functional characteristics or the biological activity of the TR17 protein. While the specification on pages 295-317, describes many potential activities for the instant TR17 protein, such as TR17 inhibition of B cell proliferation in an in vitro co-stimulatory assay (see Example 14, page 296-297), enhancement of T cell proliferation (see Example 15, page 297-298), this is a hypothetical example and there is no nexus demonstrated between administering a TR17 antibody and efficacious treatments in the claimed methods. The specification does not demonstrate that the TR17 polypeptide actually displays any of these recited activities on pages 295-317. In the absence of knowledge of the specific biological significance of the TR17 protein, there is no immediately obvious patentable use for an antibody to TR17 in the claimed methods. Since the instant specification does not disclose a "real world" use for the antibody to the TR17 protein in

the claimed methods, then the claimed invention is incomplete and, therefore, the methods do not meet the requirements of 35 USC. 101 as being useful.

A protein of unknown function would have utility if it can be employed as an indicator of a diseased state or of the presence of a disorder. One of the disclosed functions for the TR17 protein of the instant invention is that it inhibits B cell proliferation (see page 296, Example, 14). However, this is a hypothetical example and Applicants have failed to show the effect of a TR17 antibody on this function. Applicant is only required to identify one substantial credible utility and the employment of an antibody to the TR17 protein only as the subject of further research does not satisfy the utility requirement of 35 U.S.C. 101 because the courts have interpreted this statute as requiring an invention to have substantial utility where specific benefit exists in currently available form. The employment of an antibody to the TR17 protein of the instant invention, in a method of treating autoimmune disease, inhibiting B cell proliferation or inhibiting T cell function, is not a substantial or specific utility.

Applicants disclose in the specification that the claimed protein has homology to the TNF family of receptors (page 1, [0002]). The state of the art is such that functional information can be automatically derived from structural information only to a limited extent, (see Sklonick et al, Nature Biotechnology, Vol.18, No.3, pages 283-287, especially page 286, middle of column 1). Sklonick et al also state that knowledge of the overall structure or domain family is still not enough to confidently assign function to a protein. Therefore, there is little doubt that, after further characterization, the protein is found to be member of the TNF receptor family, the claimed protein would have a specific, substantial and credible utility. However, further characterization is part of the invention and until it had been undertaken, the claimed invention is

not supported by a specific asserted utility or a well established utility. The claimed invention is directed to a method of using an antibody to a TR17 polypeptide of as yet undetermined function or biological significance. Thus, since there is no biological activity disclosed for the TR17 protein, the claimed invention is not supported by either a specific and substantially asserted utility or a well established utility.

It is apparent that Applicant has failed to use sound scientific reasoning in concluding that "TR17 inhibits B cell proliferation in an in vitro co-stimulatory assay" (page 296) Accordingly, it is unclear how an antibody to TR17 could be used to treat autoimmune conditions as disparate as rheumatoid arthritis, multiple sclerosis and diabetes mellitus which are TH1 disease mediated by T cells, and systemic lupus erythematosus and Sjogren's syndrome which are mediated by B-cells (see claim 31). Furthermore, glomerulonephritis (inflamed kidney) and diabetes mellitus is not an autoimmune disease but an endocrine disorder. Therefore, Applicants are claiming treatment of unrelated diseases, which if assertions are credible, it would appear that a TR17 antibody is the "magic bullet" which medical researchers have been seeking since medical research began. This would be akin to medical research's version of the perpetual motion machine. However, given the disclosure of no data of any kind, nor the establishment of any connection or correlation of the asserted TR17 protein with any particular disease or disorder, the assertions cannot be considered credible. Accordingly, the specification fails to provide either a specific and substantial asserted utility, or a well-established utility for the TR17 protein, thus, no specific and substantial asserted utility, or a well-established utility can be established for a TR17 antibody in the claimed methods.

Claims 31 and 36-37 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantially asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The instant specification does not disclose a biological activity for the claimed protein, therefore, there is no specific and substantial asserted utility or well established for the claimed protein. The fact that the claimed nucleic acid encodes a protein that has homology to the rate decay accelerating factor protein is not sufficient to establish a specific and substantially asserted utility or a well established utility for it.

Claim Rejections - 35 USC § 112, first paragraph

4. Claims 31, 36-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn very broadly to methods of treating an autoimmune disease, inhibiting T cell proliferation and inhibiting immunoglobulin production by administering Tr17 antibody. However, the specification fails to provide any guidance for the successful inhibition of any of these conditions by using such antibody. Resolution of the various complications in regards to using any given antibody that is immunoreactive for any given protein as a therapeutic agent is highly unpredictable. One of skill in the art would have been unable to practice the invention without engaging in undue trial and error experimentation. In order to practice the invention using the specification and the state of the art as outlined below, the quantity of

experimentation required to practice the invention as claimed *in vivo* would require the *de novo* determination pharmaceutical formulations of antibody that is immunoreactive as a therapeutic agent with known antibodies against known proteins with signs, and symptoms to correlate with inhibition of the target protein. In the absence of any guidance from the specification, the amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

The specification as filed does not provide any guidance or examples that would enable a skilled artisan to use the disclosed methods of using any given TR17 antibody that is immunoreactive and as a therapeutic agent in a patient. Additionally, a person skilled in the art would recognize that predicting the efficacy of using a given antibody that is immunoreactive for a protein as a therapeutic agent *in vivo* based solely on *prophetic suggestion* as highly problematic (see MPEP §2164.02). Thus, although the specification prophetically considers and discloses general methodologies of using an antibody as a therapeutic agent, such a disclosure would not be considered enabling since the state of protein aggregation and passive immunization as highly unpredictable. The factors listed below have been considered in the analysis of enablement [see MPEP §2164.01(a) and *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)]:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The following references are cited herein to illustrate the state of the art of Sjogren's syndrome and immunization.

On the nature of passive immunization, Fox *et al.* (1997) teaches that the recent success of "biologic" agents (i.e. anti-TNF antibody and TNF receptors) in rheumatoid arthritis and of intravenous gamma globulin in various autoimmune disease suggests a potential role for these agents after "controlled trials" have been performed (see page 396, column 1, last 5 lines).

Molina et al. (1996) teach that intravenous immunoglobulin therapy has been utilized in the treatment of sensory neuropathy associated with Sjogren's syndrome.

Canhao et al. (2000) teach that intravenous gammaglobulin may be useful in the treatment of autoimmune disease (see column 2, second full para)

5. Claims 31, 36-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims require "an antibody or fragment thereof that is immunoreactive to TR17 protein" while practicing the claimed methods. The claims, however, do not require that the antibody to possess any particular conserved structure, or other distinguishing feature, such as a specific biological activity. Thus, binding to the TR17 protein draws the claims to a genus of antibodies that is defined by the desired activity to inhibit TR17 protein activity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or

chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed is a recitation of desired activity to inhibit TR17 protein. The specification does not identify any particular portion of the structure that must be conserved, nor does it provide a disclosure of structure/function correlation. The distinguishing characteristics of the claimed genus are not described. Accordingly, the specification does not provide adequate written description of the claimed genus.

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. *Vas-Cath*, 935 F.3d at 1563; see also *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); *In re Gosteli*, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572.

See *University of Rochester v. G.D. Searle & Co.*, 68 USPQ2d 1424 (DC WNY 2003) and *University of Rochester v. G.D. Searle & Co. et al.* CAFC [(03-1304) 13 February 2004]. In *University of Rochester v. G.D. Searle & Co.* a patent directed to method for inhibiting

prostaglandin synthesis in human host using an unspecified compound, in order to relieve pain without side effect of stomach irritation, did not satisfy written description requirement of 35 U.S.C. §112, since the patent described the compound's desired function of reducing activity of the enzyme PGHS-2 without adversely affecting PGHS-1 enzyme activity, but did not identify said compound, since invention consists of performing "assays" to screen compounds in order to discover those with desired effect. The patent did not name even one compound that assays would identify as suitable for practice of invention, or provide information such that one skilled in art could identify suitable compound. And since specification did not indicate that compounds are available in public depository, the claimed treatment method cannot be practiced without compound. Thus the inventors cannot be said to have "possessed" claimed invention without knowing of a compound or method certain to produce compound. Thus said patent constituted an invitation to experiment to first identify, then characterize, and then use a therapeutic a class of compound defined only by their desired properties.

Therefore the full breadth of the claim fails to meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (571) 271-0871.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
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